

Basic Investigations

Effects of Lüfukang Capsules (律复康胶囊) on Coronary Artery Ligation-Induced Arrhythmia in Dogs

HAN Li-hua 韩丽华¹, WANG Zhen-tao 王振涛¹, WU Hong 吴鸿¹, ZHANG Hui-chao 张会超¹, CHEN Shu-yin 陈舒茵², LONG Zi-jiang 龙子江³, SHEN Hong-chao 申洪超², LI Rui-ru 黎瑞汝², and LIANG Sheng-wang 梁生旺²

Objective: To observe the effects of Lüfukang Capsules (律复康胶囊 LFKC) on arrhythmia induced by ligation of coronary artery in dogs.

Methods: Thirty dogs were randomly divided into 5 groups, the model group administrated with equal volume of distilled water, the positive control group administrated with Wenxin Granules (稳心颗粒), and the small, medium and large dosage LFKC groups, 6 dogs in each group. Thirty minutes after medication, electrocardiogram was conducted and the time of arrhythmia occurrence, times of ventricular premature beat (VP), and incidence rates of ventricular tachycardia (VT) and ventricular fibrillation (VF) were recorded in the model dogs with arrhythmia induced by ligation of coronary artery.

Results: Compared with the model group, the occurrence time of arrhythmia induced by the coronary artery ligation in the medium and large LFKC groups was significantly delayed (20.45 ± 9.10 and 19.92 ± 3.78 , respectively, both $P < 0.05$). The frequency of VP in the medium and large LFKC groups was also significantly decreased (8.17 ± 6.62 and 3.83 ± 2.79 , respectively, both $P < 0.01$).

Conclusion: LFKC has anti-arrhythmic effects for the experimental arrhythmia induced by the ligation of coronary artery in dogs.

Keywords: Lüfukang Capsules (LFKC); arrhythmia; antiarrhythmics

Arrhythmia refers to the abnormalities in the frequency, rhythm and original site of cardiac impulse, which is one of the symptoms commonly seen in cardiovascular diseases. Arrhythmia not only occurs in the patients with cardiovascular diseases, but also in the patients of non-cardiovascular diseases or healthy persons. The clinical manifestations may include anxiety, palpitation, shortness of breath, weakness, chest pain, sweating, irritability, dizziness, unsound sleep, and pale or dark red tongue with petechiae and ecchymosis, and with yellow, greasy, thin white or less fur, and the pulse, knotted, intermittent, rapid, and uneven.¹

Arrhythmias may sometimes induce abnormal awareness of heart beat, making people feel only restlessness, and sometimes cause life-threatening emergencies, such as cardiac arrest or even sudden death. Rapid ventricular arrhythmia induced cardiac death is the most common cause of death in the United States, 250,000–500,000 cases die each year, accounting for 10%–20% of the adult death rate.² At present, there are many antiarrhythmics with different mechanisms. However, their clinical use is often limited by the frequent side effects, especially for the induced arrhythmic effects.^{3,4} Lüfukang Capsules (律复康胶囊 LFKC) has long been used for clinical treatment of arrhythmia with satisfactory therapeutic results, indicating that it is an effective antiarrhythmic.^{5–8} In the present study, the effects of LFKC for arrhythmia induced by ligation of

the coronary artery were investigated in dogs.

METHODS

Medicines and Reagents¹

LFKC Capsules (Batch No.080805) were made by Teaching and Research Section of Medicament, Guangdong College of Pharmacy, which were diluted with distilled water just before use. Positive control medicine Wenxin Granules (稳心颗粒 Batch No: 071007) were produced by Shandong Buchang Pharmaceutical Co. Ltd. Pentobarbital sodium (Batch No: 061206) was purchased from Beijing Chemical Reagent Co. Ltd.

Animals

Conventional thirty Beagle dogs (15 male and 15 female), weighing 8–12 kg, were supplied by Anhui Changlinhe Medical Science and Technology Co. Ltd, certificate of quality No: SCXK (皖)2006-002.

1. Henan Provincial Hospital of Traditional Chinese Medicine, Zhengzhou, Henan 450002, China; 2. Guangdong College of Pharmacy, Guangdong, Guangzhou 510006, China; 3. Anhui College of Traditional Chinese Medicine, Hefei, Anhui 230000, China

Correspondence to: Prof. HAN Li-hua, Tel: 86-371-60908801, E-mail: hlh@ sina.com, Fax: 86-371-60908800

This study was supported by Plan for Science and Technology Innovation Talented Persons of Henan Province of China (No. 0621002700).

Instruments

Animal respirator was produced by Chengdu Taimeng Science and Technology Co. Ltd; XD-7100 electrocardiograph was made by Shanghai Medical Electronic Instrument Factory.

Animal Modeling and Grouping

The experiment complied with the Animal Management Rule of the Ministry of Health, PRC, and the experimental protocol was approved by the Animal Care Committee of Guangdong College of Pharmacy. Thirty Beagle dogs were housed at the Animal Care Center of Guangdong College of Pharmacy.

The arrhythmia model was prepared with a modified method according to previous description.⁹ Five days after adaptive feeding, each animal was anesthetized with 0.8% pentobarbital sodium via intraperitoneal injection, followed by endotracheal intubation, and mechanical ventilation. After thoracotomy, the heart was exposed and the left anterior descending branch of coronary artery was ligated with a complete and permanent occlusion, resulting in acute myocardial infarction. Additionally, an arterial catheter with heparin was inserted from the femoral artery to the abdominal aorta for continuous measurement of the arterial blood pressure. After the chest wall was sutured and artificial respiration was stopped, the dogs were transferred to specialized cages. The dogs were randomly divided (using random number table) into five groups: the model group, the positive control group, and the small, medium and large dose LFKC groups, 6 dogs (3 male and 3 female) in each group.

Medicine Dosages and Administration Methods

For the small dose LFKC group, 0.53 g crude drug/kg was intragastrically administrated, once per day. The dosage corresponded to 1 time of the clinical human dose according to the body surface area, or 1.6 times of clinical 60-kilogram adult dosage according to the body weight. Just before use, the contents of the LFKC Capsules were prepared into 1.91% solution with distilled water, which contained 10.60% crude drug, and 5 mL/kg was given each time.

For the medium dose LFKC group, 1.060 g crude drug/kg was intragastrically administrated, once per day. The dosage corresponded to 2 times of the clinical human dose according to the body surface area, or 3.2 times of clinical 60-kilogram adult dosage according to the body weight. Just before use, the contents of the LFKC Capsules were prepared into 3.82% solution with

distilled water, which contained 21.20% crude drug and 5 mL/kg was given each time.

For the large dose LFKC group, 2.120 g crude drug/kg was intragastrically administrated, once per day. The dosage corresponded to 4 times of clinical human dose according to the body surface area, or 6.4 times of clinical 60-kilogram adult dosage according to the body weight. Just before use, the contents of the LFKC Capsules were prepared into 7.64% solution with distilled water, which contained 42.40% crude drug and 5 mL/kg was given each time.

For the positive control group, 1.440 g crude drug/kg was intragastrically administrated, once per day. The dosage corresponded to 2 times of the clinical human dose according to the body surface area, or 3.2 times of clinical 60-kilogram adult dosage according to the body weight. Just before use, Wenxin Granules were prepared into 28.80% solution with distilled water, and 5 mL/kg was given each time.

For the model group, 5 mL/kg distilled water was intragastrically administrated, once each day.

Thirty min after intragastric administration, the left anterior descending branch of coronary artery was ligated.

Indexes of Observation

After the end of modeling, ECG was immediately conducted, and the time of arrhythmia occurrence, times of ventricular premature beats (VP) in one min, and incidence rates of ventricular tachycardia (VT) and ventricular fibrillation (VF) were recorded and calculated.

Statistical Analysis

The data were processed with software of SPSS, v12.0 (SPSS Inc., Chicago, IL, USA) for windows, and expressed as $\bar{X} \pm s$. Differences between two groups were assessed by unpaired Student's *t*-test, and one-way ANOVA was used for comparison among multiple groups. $P < 0.05$ was regarded as statistically significant difference.

RESULTS

As shown in the Table 1, LFKC significantly delayed the time of arrhythmia occurrence in coronary artery-ligated dogs, and reduced the times of VP and the incidence rates of VT and VF, with significant differences as compared with the model group ($P < 0.01$ or 0.05).

Table 1. Effects of LFKC on arrhythmia induced by ligation of coronary artery in dogs ($\bar{X} \pm s$, $n=30$)

Groups	Dosage (g/kg)	Time of arrhythmia occurrence (min)	Times of VP	Rate of VT (%)	Rate of VF (%)
Model	—	8.73±8.26	30.67±15.31	33.3	16.7
Positive control	1.440	22.17±9.24*	9.67±12.23*	16.7	0
Small LFKC dose	0.530	12.90±6.83	14.50±9.73	16.7	0
Medium LFKC dose	1.060	20.45±9.10*	8.17±6.62**	16.7	16.7
Large LFKC dose	2.120	19.92±3.78*	3.83±2.79**	0	0

Notes: Compared with the model group, * $P < 0.05$, ** $P < 0.01$.

SUMMARY

According to the TCM theories, *qi* and blood are the fundamental substances for nourishing the heart. People with congenital deficiency, or infirm with age and prolonged diseases, are susceptible to arrhythmias because of the damage of *qi* and blood. LFKC is the authors' experiential prescription for treating arrhythmia, which is composed of Hongshen (Radix Ginseng Rubra), Maidong (Radix Ophiopogonis), Shashen (Radix Adenophorae), Longyanrou (Dried Longan Pulp), Suanzaoren (Spine Date Seed), Danshen (Radix Salviae Miltiorrhizae), Wuweizi (Fructus Schisandrae) and Longchi (Fossilia Dentis Mastodi), etc. In the recipe, Hongshen (Radix Ginseng Rubra) and Longyanrou (Dried Longan Pulp) functions to enrich the heart blood; Shashen (Radix Adenophorae) and Maidong (Radix Ophiopogonis) can reinforce the heart-yin; Suanzaoren (Spine Date Seed) has the effect of invigorating the heart-*qi*; Sheng Longchi (Fossilia Dentis Mastodi) may tranquilize the mind; Danshen (Radix Salviae Miltiorrhizae) can promote and regulate the flow of *qi* and blood. So, the whole recipe has functions of supplementing *qi* and nourishing yin, nourishing the blood to tranquilize the mind, resuming regular heart rate and relieving palpitation.

The results from the present study show that LFKC can significantly delay the time of arrhythmia occurrence, reduce the frequency of VP and decrease the occurrence rates of VT and VF in the dog with coronary artery ligation, exerting better antiarrhythmic effects as compared with Wenxin Granules, which can be used for preventing cardiac sudden death and other major cardiac events.¹⁰

REFERENCES

1. Shi H, Long ZJ, Wang J. Advances of clinical and experimental studies in traditional Chinese medicine and drugs for treatment of arrhythmia. *Anhui Med Pharm J (Chin)* 2009; 13: 95-97.
2. Spooner PM, Albert C, Benjamin EJ, Boineau R, Elston RC, George AL Jr, et al. Sudden cardiac death, genes, and arrhythmogenesis: consideration of new population and mechanistic approaches from a national heart, lung, and blood institute workshop, part I. *Circ* 2001; 103: 2361-2364.
3. Zhu YR, Cao DF. Induction or exacerbation of arrhythmia by antiarrhythmics. *Pacing Heart (Chin)* 1988; 2: 210-212.
4. Darbar D, Roden DM. Pharmacogenetics of antiarrhythmic therapy. *Expert Opin Pharmacother* 2006; 7: 1583-1590.
5. Han LH, Zhang Y. Study on antiarrhythmic action of Lüfukang Capsules. *Study Tradit Chin Med (Chin)* 1998; 11: 13-16.
6. Han LH, Wang SF. Clinical observation on Lüfukang Capsules for treatment of arrhythmia of both *qi* and yin deficiency type in 100 cases. *Henan J Tradit Chin Med Pharm (Chin)* 1998; 13: 48-49.
7. Wang SF, Yang CY. Clinical study on Lüfukang Capsules for treatment of arrhythmia. *Jiangsu J Tradit Chin Med (Chin)* 1999; 20: 9-10.
8. Han LH, Zhang HC. Treatment of 36 cases of functional ventricular premature beat with Lüfukang Capsules. *World Chin Med Pharm (Chin)* 2009; 4: 143.
9. Kulier AH, Novalija E, Hogan Q, Vicenzi MN, Woehlck HJ, Bajic J, et al. The effects of the new antiarrhythmic E 047/1 on postoperative ischemia-induced arrhythmias in dogs. *Anesth Analg* 1999; 89: 1393-1399.
10. Yang YL, Liu RF. Advances of mechanism and clinical treatment of arrhythmia with Wenxin Granules. *China J Misdiagnosis Sci (Chin)* 2009; 9: 2784-2785.

(Received May 12, 2010)